

WHAT IS CLAIMED IS:

- 1 1. A method for identifying rare events in a biological
2 sample, comprising:
 - 3 obtaining a source of cells;
 - 4 contacting the source with a binding agent specific
5 for a cell specific marker associated with a rare event
6 wherein the binding agent is bound to a magnetic bead and
7 wherein the binding agent binds to cells in the source
8 expressing the cell specific marker;
 - 9 separating cells bound by the binding agent from the
10 source thereby obtaining a sub-population of cells enriched
11 for the cell specific marker associated with the rare event;
 - 12 placing the enriched sample on a substrate;
 - 13 automatically scanning the substrate at a plurality
14 of coordinates;
 - 15 automatically obtaining a plurality of images at
16 locations on the substrate that comprise the enriched sample;
 - 17 and
 - 18 processing the plurality of image to identify the
19 rare event.
- 20
- 21 2. The method according to claim 1, wherein the binding
22 agent is an antibody.
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- 24 3. The method according to claim 1, wherein the sub-
25 population is enriched for carcinoma cells.
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- 27 4. The method of claim 1, wherein the separating is done by
28 positive selection.
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30 5. The method of claim 1, wherein the separating is done by
31 negative selection.

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33 6. The method of claim 2, wherein the antibody is monoclonal
34 or polyclonal.

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36 7. The method of claim 2, wherein the antibody recognizes an
37 epithelial marker.

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39 8. The method of claim 2, wherein the antibody is selected
40 to avoid cross reactivity with the beads.

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42 9. The method of claim 3, wherein the carcinoma cells are
43 from peripheral blood.

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45 10. The method of claim 1, further comprising:
46 (a) automatically identifying a coordinate of the rare event;
47 and
48 (b) automatically acquiring an image of the rare event, at the
49 location coordinates.

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51 11. The method of claim 1, wherein the rare event is detected
52 by immunohistochemistry.

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54 12. The method of claim 1, wherein the rare event is detected
55 by in situ hybridization.

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57 13. The method of claim 1, wherein the rare event is detected
58 by a stain.

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60 14. The method of claim 13, wherein the stain is a nucleic
61 acid dye selected from the group consisting of hematoxylin,

Giemsa stain, methyl green, Nuclear Fast-Red, Hoechst 33342, Hoechst 33258, thiazole orange, DAPI, ethidium bromide, propidium iodide, TOTO, YOYO-1, SYTOX Blue, SYTOX Green, 7-Aminoactinomycin, 9-Amino-6-chloro-2-methoxyacridine, and acridine homodimer.

15. The method of claim 13, wherein the rare event is stained with a cytoplasmic dye such as eosin or Kleihauer-Betke cytochemical stain or a combination thereof.

16. The method of claim 1, wherein the cell specific marker is detected by a nuclear stain and counterstain.

17. The method of claim 1, wherein the cell specific marker is detected by immunohistochemistry, in situ hybridization, staining or a combination thereof.

18. The method of claim 1, wherein the image is a digital image.